•••								
		2003/08/12 10:39	USPAT; US-PGPUB; EPO; JPO; DERWENT	(10 or 11) and 5	2	L12	BRS	12
		2003/08/12 10:39	USPAT; US-PGPUB; EPO; JPO; DERWENT	bajwa adj kamaljit.in.		L11	BRS	11
		2003/08/12 10:38	USPAT; US-PGPUB; EPO; JPO; DERWENT	shirley adj bret.in.	14	L10	BRS	10
		2003/08/12 10:38	USPAT; US-PGPUB; EPO; JPO; DERWENT	5 same (7 or 8)	—	L9	BRS	9
		2003/08/12	USPAT; US-PGPUB; EPO; JPO; DERWENT	"200" adj mg/ml	1963	L8	BRS	∞
Erro r Defi Err s nitio	Com ments	Time Stamp	DBs	Search Text	Hits	L#	Туре	

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FILE 'MEDLINE' ENTERED AT 10:43:56
                                               12 AUG 2003
  FILE 'CAPLUS' ENTERED AT 10:43:56 ON 12 AUG 2003
  USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
  COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
  FILE 'BIOSIS' ENTERED AT 10:43:56 ON 12 AUG 2003
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 FILE 'EMBASE' ENTERED AT 10:43:56 ON 12 AUG 2003
 COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.
 FILE 'SCISEARCH' ENTERED AT 10:43:56 ON 12 AUG 2003
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 FILE 'AGRICOLA' ENTERED AT 10:43:56 ON 12 AUG 2003
 => s (insulin-like growth factor-1) or IGF-1
            29701 (INSULIN-LIKE GROWTH FACTOR-1) OR IGF-1
 => s arginine or guanidine or guanidium
           406219 ARGININE OR GUANIDINE OR GUANIDIUM
 => s 12 (p) solubiliz?
             2954 L2 (P) SOLUBILIZ?
 => s 11 (p) 13
                 5 L1 (P) L3
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 PROCESSING COMPLETED FOR L4
                  2 DUPLICATE REMOVE L4 (3 DUPLICATES REMOVED)
 => d 15 1-2 ibib abs
       ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
                               1999:325815 CAPLUS
 ACCESSION NUMBER:
 DOCUMENT NUMBER:
                               130:343031
 TITLE:
                               Compositions providing for increased IGF-I solubility
 INVENTOR(S):
                               Shirley, Bret A.; Bajwa, Kamaljit
 PATENT ASSIGNEE(S):
                               Chiron Corporation, USA
 SOURCE:
                               PCT Int. Appl., 32 pp.
                               CODEN: PIXXD2
DOCUMENT TYPE:
                               Patent
LANGUAGE:
                               English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
      PATENT NO.
                           KIND DATE
                                                    APPLICATION NO. DATE
              4063 A1 19990520 WO 1998-US23673 19981106
AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, RV, KG, KZ, MD, BU, TJ, TM
      wo 9924063
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93 A1 19990531 AU 1999-
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                                                    ÁU 1999-15193
                                                                         19981106
      EP 1028748
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                                                    EP 1998-959383
                                                                         19981106
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                            В1
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                                  20030515
                                                    AT 1998-959383
                                                                         19981106
PRIORITY APPLN. INFO.:
                                                US 1997-64891P
                                                                        19971107
                                                wo 1998-us23673 w 19981106
      IGF-I compns. include a solubilizing compd. comprising a guanidinium group
AB
      that provides for IGF-I compns. in which IGF-I is highly sol. at phs of
      about 5.5 or greater and at refrigerated temps. IGF-I was formulated with
```

arginine for injection.

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECO ALL CITATIONS AVAILABLE IN THE FORMA REFERENCE COUNT: ANSWER 2 OF 2 MEDLINE on STN **DUPLICATE 1** ACCESSION NUMBER: 92316967 MEDLINE PubMed ID: 1618780 DOCUMENT NUMBER: 92316967 Enhanced insulin-induced mitogenesis and mitogen-activated TITLE: protein kinase activities in mutant insulin receptors with substitution of two COOH-terminal tyrosine autophosphorylation sites by phenylalanine. Ando A; Momomura K; Tobe K; Yamamoto-Honda R; Sakura H; Tamori Y; Kaburagi Y; Koshio O; Akanuma Y; Yazaki Y; + **AUTHOR:** Third Department of Internal Medicine, Faculty of Medicine, CORPORATE SOURCE: University of Tokyo, Japan. JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Jun 25) 267 (18) SOURCE: 12788-96. Journal code: 2985121R. ISSN: 0021-9258. PUB. COUNTRY: **United States** DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) LANGUAGE: English FILE SEGMENT: ENTRY MONTH: Priority Journals

199208.

ENTRY DATE:

Entered STN: 19920815

Last Updated on STN: 20000303

Entered Medline: 19920806
We have studied the function of a mutant human insulin receptor in which AB two COOH-terminal autophosphorylation sites (Tyr-1316 and -1322) were replaced by phenylalanine (F/Y COOH-terminal 2 tyrosines (CT2)). In addition, we have also constructed a mutant receptor in which Lys-1018 in the ATP-binding site was changed to ***arginine*** (R/K 1018). Both the wild type insulin receptor (HIR) and the mutant receptors were expressed in Chinese hamster ovary (CHO) cells by stable transfection. Autophosphorylation of ***solubilized*** and partially purified F/ and partially purified F/Y CT2 was decreased by approximately 30% compared with the HIR. Tyrosine kinase activities of F/Y CT2 and HIR toward exogenous substrates were almost equal. When CHO cells transfected with F/Y CT2 (CHO-F/Y CT2) were stimulated with insulin, autophosphorylation of the beta-subunit of the insulin receptor and the phosphorylation of an endogenous substrate (pp185) in the intact cell were normal compared with cells expressing HIR (CHO-HIR). CHO-F/Y CT2 exhibited the same insulin sensitivity as CHO-HIR with respect to 2-deoxyglucose uptake. However, the dose-response curve of insulin-stimulated thymidine incorporation in CHO-F/Y CT2 was shifted to the left (approximately 5-7-fold) compared with that in CHO-HIR. There was no significant difference in ***insulin*** - ***like*** ***factor*** ***1*** -stimulated thymidine ***growth*** incorporation between CHO-F/Y CT2 and CHO-HIR. Furthermore, the dose-response curve of insulin-stimulated kinase activity toward myelin basic protein in CHO-F/Y CT2 was also shifted to the left (approximately 5-fold) compared with that in CHO-HIR. Kinase assays in myelin basic protein-containing gels revealed that both species of MAP kinases (M(r) 44,000, 42,000) were more sensitive to activation by insulin in CHO-F/Y CT2 than in CHO-HIR. This observation was confirmed in immune complex kinase assays toward microtubule-associated protein 2 (MAP2) using specific antibodies against mitogen-activated protein (MAP) kinase. 1018 mutant insulin receptors showed an absence of insulin-stimulated kinase activity and CHO cells transfected with R/K 1018 (CHO-R/K 1018) failed to enhance 2-deoxyglucose uptake or thymidine incorporation in response to insulin. In addition, R/K 1018 kinase-defective insulin receptors were unable to mediate insulin-stimulated MAP kinase activation. These data suggest that: 1) tyrosine kinase activity of the insulin receptor is required for activation of insulin-stimulated MAP kinases and 2) phosphorylation of COOH-terminal tyrosine residues may play an inhibitory role in mitogenic signaling through regulation of MAP kinases.

=> d his

(FILE 'HOME' ENTERED AT 10:43:34 ON 12 AUG 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT $10\!:\!43\!:\!56$ ON 12 AUG 200329701 S (INSULIN-LIKE GROWTH FACTOR-1) OR IGF-1 406219 S ARGININE OR GUANIDINE OR GUANIDIUM 2954 S L2 (P) SOLUBILIZ? 5 S L1 (P) L3 2 DUPLICATE REMOVE L4 (3 DUPLICATES REMOVED)

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=> s (12 mg/ml) or (200 mg/ml)
      IS NOT A VALID FIELD CODE
      IS NOT A VALID FIELD CODE
 ML'
      IS NOT A VALID FIELD CODE
      IS NOT A VALID FIELD CODE
                0 (12 MG/ML) OR (200 MG/ML)
 => s shirley bret/au
                6 SHIRLEY BRET/AU
=> s bajwa kamaliit/au
L8
               2 BAJWA KAMALJIT/AU
 => s (17 or 18) and 11
                3 (L7 OR L8) AND L1
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KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L9
                 3 DUPLICATE REMOVE L9 (0 DUPLICATES REMOVED)
=> d 110 1-3 ibib abs
    ANSWER 1 OF 3
                       BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
                       2003:313118 BIOSIS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                       PREV200300313118
                       Method for producing sustained-release formulations.
    ***Shirley, Bret*** ; Hora, Maninder; O'Hagan, Derek;
TITLE:
AUTHOR(S):
                       Singh, Manmohan
                       ASSIGNEE: Chiron Corporation
PATENT INFORMATION: US 6573238 June 03, 2003
SOURCE: Official Gazette of the United States Patent and Trademark
                       Office Patents, (June 3 2003) Vol. 1271, No. 1, pp. No
                       Pagination. http://www.uspto.gov/web/menu/patdata.html.
                       ISSN: 0098-1133.
DOCUMENT TYPE:
                       Patent
LANGUAGE:
                       English
      Methods for preparing biodegradable microparticles are provided. Also
      provided are microparticles prepared by the method which include
      ***IGF*** - ***1*** entrapped therein. The microparticles allow for controlled release of ***IGF*** - ***1*** and other polypeptides
                                                             and other polypeptides
      over prolonged periods of time.
     ANSWER 2 OF 3 CAPLUS
                               COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:
                             1999:325815 CAPLUS
DOCUMENT NUMBER:
                             130:343031
                            Compositions providing for increased IGF-I solubility Shirley, Bret A.; ***Bajwa, Kamaljit***
TITLE:
INVENTOR(S):
PATENT ASSIGNEE(S):
                             Chiron Corporation, USA
SOURCE:
                             PCT Int. Appl., 32 pp.
                             CODEN: PIXXD2
DOCUMENT TYPE:
                             Patent
LANGUAGE:
                             English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                         KIND
                                DATE
                                                 APPLICATION NO.
                                                                     DATE
     wo 9924063
                          Α1
                                19990520
                                                 WO 1998-US23673
                                                                     19981106
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AT 238807

20011120

20030515

JP 2000-520151 19981106 AT 1998-959383 19981106

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PRIORITY APPLN. INFO.:
                                                   US 1997-64891P
                                                                            19971107
                                                   wo 1998-us23673 w 19981106
        IGF-I compns. include a solubilizing compd. comprising a guanidim um group
  ΔR
        that provides for IGF-I compns. in which IGF-I is highly sol. at phs of
        about 5.5 or greater and at refrigerated temps. IGF-I was formulated with
         arginine for injection.
  REFERENCE COUNT:
                                        THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                                        RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
  L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
  ACCESSION NUMBER:
                                 1999:325813 CAPLUS
  DOCUMENT NUMBER:
                                 130:343029
  TITLE:
                                Method for producing
                                                             ***IGF***
                                                                         - ***1***
                                 sustained-release formulations
  INVENTOR(S):
                                   ***Shirley, Bret***
                                                             ; Hora, Maninder; O'Hagan,
                                Derek; Singh, Manmohan
  PATENT ASSIGNEE(S):
                                Chiron Corporation, USA
  SOURCE:
                                PCT Int. Appl., 60 pp.
                                CODEN: PIXXD2
  DOCUMENT TYPE:
                                Patent
  LANGUAGE:
                                English
  FAMILY ACC. NUM. COUNT:
  PATENT INFORMATION:
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                                                                          19981106
 PRIORITY APPLN. INFO.:
                                                  US 1997-64891P
                                                                     Ρ
                                                                          19971107
                                                  US 1998-96066P
                                                                          19980811
                                                  WO 1998-US23627 W
                                                                          19981106
       Methods for prepg. biodegradable poly(D,L-lactide-co-glycolide)
 AB
       microparticles are provided. Also provided are microparticles prepd. by the method which include ***IGF*** - ***1*** entrapped therein. The microparticles allow for controlled release of ***IGF*** - ***1***
       and other polypeptides over prolonged periods of time.
 REFERENCE COUNT:
                                      THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
                                      RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> d his
      (FILE 'HOME' ENTERED AT 10:43:34 ON 12 AUG 2003)
      FILE 'MEDLINE, CAPLUS, 10:43:56 ON 12 AUG 2003
                                 BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
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L1
           406219 S ARGININE OR GUANIDINE OR GUANIDIUM
L2
L3
             2954 S L2 (P) SOLUBILIZ?
5 S L1 (P) L3
L5
                   DUPLICATE REMOVE L4 (3 DUPLICATES REMOVED)
L6
                   S (12 MG/ML) OR (200 MG/ML)
                   S SHIRLEY BRET/AU
L8
                 2 S BAJWA KAMALJIT/AU
                     (L7 OR L8) AND L1
L10
                 3 DUPLICATE REMOVE L9 (0 DUPLICATES REMOVED)
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COST ĬN U.S. DOLLARS
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L7

L9

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE ENTRY -1.95

STN INTERNATIONAL LOGOFF AT 10:50:32 ON 12 AUG 2003